A16
CON'T

determining a temporal difference image value based upon said correlation output values.

REMARKS

This amendment is in response to the Office Action dated 4/9/03. Also enclosed are a Terminal Disclaimer and an Associate Power of Attorney. Entry of this Amendment and reconsideration of this application are respectfully requested. The amendments are also given in the older format, with insertions and deletions, in Attachment A following these remarks.

Objections to the Specification

Each of the Examiner's objections to the specification have been addressed. Each requested correction has been made, as indicated in the amended paragraphs above.

Claim 16 was objected to due to a typographical error. Correction has been made.

Objections to the Drawings

The Examiner correctly noted that reference number "82" in figure 4 should be changed to "22". The Examiner also noted that FIG. 7 was not included with the specification.

In response, a new set of drawings is enclosed: the correction to FIG. 4 has been made, and FIG. 7 is included in the set.

Double Patenting

Claims 1-22 were rejected under the judicially-created doctrine of obviousness-type double patenting, over a patent to Burke et al. (U.S. Patent No. 6,351,660), or over Burke in

combination with one or more other patents.

In response, a terminal disclaimer in compliance with 37 C.F.R. §1.321(c) is enclosed, which disclaims the terminal part of the statutory term of any patent granted on the instant application, which would extend beyond the expiration date of the full statutory term of U.S. Patent No. 6,351,660. Note that U.S. Patent No. 6,351,660 and the present application are commonly assigned to Litton Systems, Inc.

It is believed that the filing of the enclosed terminal disclaimer overcomes the Examiner's double patenting rejections.

Claim Rejections

Rejections under §102

Claims 1 and 9-10 were rejected as anticipated by a patent to Yanagita et al.

Claim 1

In response, claim 1 has been amended to better clarify the differences between the applicants' invention and that which is disclosed in Yanagita.

As amended, claim 1 is directed to a method of visually documenting historical changes in biological tissue. The method comprises the steps of:

(a) obtaining a first image of a region of tissue;

(b) after obtaining the first image, obtaining a second image of the region of tissue;

(c) digitally storing the first and second images as digitized first and second images;

(d) spatially adjusting at least one of the first and second digitized images to spatially register the images so that corresponding features in both images are mapped to corresponding positions; and

(e) creating from the first and second digitized images a derived image which visually emphasizes temporal differences between the first and second images, thereby visually emphasizing historical changes between the images.

Support for this amendment is found in the specification at, for example, page 7, lines 21-24.

The applicants' usage of "temporal differences" as recited in claim 1 is essential to their method, and represents a very significant distinction with respect to the cited art. "Temporal difference" learning is a particular technique known to those familiar with the art of tracking historical changes using time-separated images (see, e.g., http://www-anw.cs.umass.edu/~rich/book/the-book.html (MIT Press, Cambridge, MA 1998) for a discussion of temporal difference learning). A temporal difference image provides a scalar or reinforcement metric of learning; it is a reinforcement feedback signal indicating a scalar of how good/bad, how much change (vector), or how strongly (acceleration) an action is happening. The scalars may represent, for example, a natural change, or the effectiveness of a treatment. For example, if digitized two dimensional images are considered, the images are preferably first normalized to a common average value, then corresponding pixels are subtracted and the temporal difference values stored in a corresponding position in a temporal difference image. Analogously, if three-dimensional imagery is available (which is greatly preferred), voxels at corresponding locations in the early and later images are subtracted one from the other, and the result stored in a voxel of a temporal difference (volume) image. Thus, normalized "before" and "after" images can be subtractively compared, voxel-by-voxel, to obtain a three-dimensional temporal difference image which represents the temporal differences between the before and after images.

Support for the assertion that temporal difference learning as described above is the technique to which the applicants are referring in the amended claims can be found in the specification at, for example, on page 7, line 21 to page 8, line 25, and on page 11, line 23 to page 13, line 10.

This is much different from the method disclosed in Yanagita. As shown in his FIG. 2 and described at column 8, lines 13-36, Yanagita performs basic <u>subtraction processing</u> between sequentially-acquired images. Subtraction processing provides a simple difference image, which can only be used to determine whether or not a change has occurred. This is <u>not</u> the same as the temporal difference image processing required by the amended claim.

Yanagita is directed to a DISPLAY SYSTEM ("Image Displaying Apparatus"), that can switch between temporally sequenced images that have been stored in memory, as well as between subtraction images. Subtraction images do show differences between sequential images, but the images must be interpreted by the observer as a vector or by additional processing. In other words, Yanagita's subtraction images provide good graphics, but no metrics or other direct scientific information.

In contrast, the applicants' method provides temporal information processing, which is capable of displaying temporal difference information over the associated image. This method provides tangible measures of changes that may have occurred over time. What Yanagita displays is open to interpretation and judgment, whereas the applicants' method provides temporal difference values that can be applied to limits, thresholds, ranges, rates of change, or other preset parameters that can be applied via analog or digital processing.

An example which illustrates the difference between the methods might be helpful. Say a patient has a bleeder (aneurysm)

in an eye. A dye is injected into a nearby artery. Using Yanagita's method here results in a subtraction image which shows blood in the intraocular region. In contrast, the applicants' method provides temporal difference information which could indicate, for example, the rate and direction of blood flow, and/or the size (associated with rate) of the hole in the artery, and the 3D location around the vessel.

In sum, there is a vast difference between Yanagita's approach and that of the applicants, with the applicants utilizing a much more complex and sophisticated analysis method (temporal difference information processing), which yields substantially more information than does the Yanagita apparatus.

A claim is anticipated when every one of its elements is disclosed in a single prior art reference. As has been shown above, Yanagita does not disclose the temporal difference processing required in the amended claim 1. Thus, Yanagita cannot and does not anticipate the amended claim 1, which is therefore allowable over Yanagita.

Note that the specification has been amended to more explicitly describe aspects of the invention's use of temporal differences. The added text is either implicit in the discussion found in the original application, or concerns inherent characteristics of temporal difference learning which would be well known to those of ordinary skill in the art. No new matter has been added.

<u>Claims 9 and 10</u>

Each of claims 9 and 10 depend from the amended claim 1, and are therefore allowable on that basis. In addition, each of claims 9 and 10 has been amended to better clarify its

differences with respect to the cited art, such that these claims are also allowable on independent grounds.

The amended claim 9 is directed to a method of creating the composite image of claim 1, which requires the determination of a "temporal difference image value based upon the temporal difference between said image intensity at said location in said first image and the respective intensity at said corresponding location in said second image." As discussed above, Yanagita fails to disclose the use of temporal difference image values are required by the amended claim 9. Claim 9 is thus allowable on this independent basis.

The amended claim 10 also requires the use of temporal image differences, which are not disclosed or suggested in the Yanagita patent. Claim 10 is thus allowable on this independent basis.

Rejections under §103

Claims 2-3 and 5-6

Claims 2-3 and 5-6 were rejected as obvious over Yanagita in view of Kawachi et al.

Each of claims 2-3 and 5-6 depends from the amended claim 1, and are thus allowable along with claim 1.

Claim 7

Claim 7 was rejected as obvious over Yanagita and Kawachi and further in view of Wang.

Claim 7 depends from the amended claim 1, and is thus allowable along with claim 1.

Claim 8

Claim 8 was rejected as obvious over Yanagita and Kawachi and further in view of Mitchell et al.

Claim 8 depends from the amended claim 1, and is thus allowable along with claim 1.

Claims 4 and 19-21

Claims 4 and 19-21 were rejected as obvious over Yanagita and Kawachi and further in view of Trezza.

Claim 4 depends from the amended claim 1, and is thus allowable along with claim 1.

Claim 19 is an independent claim, which has been amended to better clarify its differences with respect to the cited art.

As amended, claim 19 is directed to a system for enhancing imagery of bodily tissues by relating earlier and later images, comprising:

- an image processor, programmed to:

- (a) receive the earlier and later images,

- (b) register the earlier and later images by controlling an optical correlator to find a position of correlation between the earlier and later images,

- (c) derive a composite image from the earlier and later images,

- (d) compute temporal differences between the earlier and later images, and

- (e) emphasize the temporal differences in said composite image; and

- an optical correlator coupled to said image processor and arranged to correlate said earlier and later images, and to output to said image processor a cross correlation image which is indicative of the position of correlation of the processed images.

As noted above, the patent to Yanagita fails to disclose anything related to temporal difference image processing,

including the computing or the emphasizing of temporal differences between images as required by the amended claim 19. The citations to Kawachi and Trezza do nothing to cure these deficiencies, as they also fail to disclose a system capable of performing the recited functions.

As such, the invention recited in the amended claim 19 would not have been obvious at the time the invention was made in view of Yanagita, Kawachi and Trezza. Claim 19 is thus allowable.

As the limitations of claim 20 were largely incorporated into the amended claim 19, claim 20 has been canceled.

The amended claim 19 is the parent of claim 21, which is therefore allowable along with claim 19.

Claim 22

Claim 22 was rejected as obvious over Yanagita, Kawachi, Trezza and Wang.

Claim 22 depends from the amended claim 19, and is thus allowable along with claim 19.

Claims 11-13 and 16

Claims 11-13 and 16 were rejected as obvious over Yanagita in view of a patent to Gur et al.

Claim 11 is an independent claim, which has been amended to better clarify its differences with respect to the cited art.

As amended, claim 11 is directed to a method of creating a displayable composite mammographic image from a plurality of raw mammographic images, corresponding to earlier and later mammographic images, comprising the steps of:

- (a) obtaining the earlier image of a region of tissue;

- (b) obtaining the later image of substantially the same region of tissue;

- (c) deriving a temporal difference image which represents changes between the earlier and later images; and

- (d) combining at least one of the earlier and later images with the temporal difference image, to produce a composite image.

As noted above, the patent to Yanagita fails to disclose or suggest anything related to temporal difference images, including the deriving or combining of such images as required by the amended claim 11. The citation to Gur does nothing to cure these deficiencies, as it also fails to disclose the use of the recited methods.

As such, the invention recited in the amended claim 11 would <u>not</u> have been obvious at the time the invention was made in view of Yanagita and Gur. Claim 11 is thus allowable.

Each of claims 12-13 and 16 depends from amended claim 11, and are thus allowable along with claim 11.

<u>Claim 14</u>

Claim 14 was rejected as obvious over Yanagita, Gur and Wang.

Claim 14 depends from the amended claim 11, and is thus allowable along with claim 11.

<u>Claim 15</u>

Claim 15 was rejected as obvious over Yanagita, Gur and Mitchell.

Claim 15 depends from the amended claim 11, and is thus allowable along with claim 11.

Claim 17-18

Claims 17-18 were rejected as obvious over Yanagita, Gur and Kawachi.

Claims 17-18 depend from the amended claim 11, and are thus allowable along with claim 11.

New claim

A new claim, claim 23, has been added. Claim 23 depends from claim 4, and recites a combination of elements not disclosed in any of the cited art.

All of the claims presently in the application are believed to be patentably distinct with respect to the cited art and to otherwise be in proper form for allowance. A Notice of Allowance is respectfully requested.

Respectfully submitted,

July 3, 2003

Steven C. Patrick
Registration No. 40,341
Attorney for Applicant

KOPPEL, JACOBS, PATRICK & HEYBL
555 St. Charles Drive, Suite 107
Thousand Oaks, California 91360
(805)373-0060

Attachment A:

Amended specification with insertions and deletions indicated:

Paragraph at page 2, lines 13-20:

An image processing system and method visually documents historical changes in a medical image by processing and comparing historical with later images. A composite image is created which visually emphasizes the temporal differences between historical and later images. Preferably three-dimensional, digitized images, displayable in various projections, are stored for archival purposes on computer readable media.

Paragraph at page 2, lines 21-32:

To properly relate the historical and later images, an image processor preferably exploits an optical correlator to register the images accurately, by finding a transformation which produces a pre-determined degree of correlation between the images, then adjusting one image accordingly. The images are then compared, preferably volume element by volume element ("voxel by voxel") , to detect temporal differences between historical and later images. A composite image is displayed with synthetic colors or other visual clues to emphasize [apparent changes] the scalars in the imaged tissue, based on temporal differences between the historical and later images.

Paragraph at page 5, line 16 through page 6, line 2:

Next, in step 52, pathological feature data is preferably loaded by the image processor 24 (preferably from a data network but alternatively by retrieval from storage or through another input channel). The pathological feature data is useful for narrowing the region of interest for image processing, and could be provided in any of several useful forms. Typically, a

physical region of interest (ROI) in the historical image has been previously identified by a radiologist or other professional, and the coordinates of that region recorded in association with the historical image. In that case, the coordinates of the ROI are the pathological feature data. Alternatively, certain image shapes or characteristics, stored in a pathological image library, could be compared with the current image by image correlation to define the pathological region as described below in connection with FIGs. 6a -6c. A further alternative is to employ known automated methods for the detection of abnormalities in digital mammograms. For example, see U.S. Patent No. [5,4;91,627] <u>5,491,627</u> to Zhang et al. (1996). The locations of any detected suspect lesions, as determined by such an automated method, could be used as the pathological feature data to identify and locate the ROI in the image.

Paragraph between page 6, line 30 and page 7, line 9:

Next, to obtain improved registration between the historical and new image, the image processor correlates the pathological feature set with the new image (step 58), preferably by the method described below in connection with FIGs. 5a and 5b. The information gained from the correlation operations allows better registration of the new image with the historical imagery and defines an ROI in the new image. <u>This approach to 'better' registration provides for improved temporal difference resolution, and makes the associate measures more accurate within the region of interest.</u> The ROI thus defined is then re-scanned (step 60), preferably as described above, with scanning ultrasound equipment but with a finer level of resolution. Finer resolution can be obtained by using slower scan speeds, higher frequency ultrasound, finer and more numerous receive sensors, or other techniques as known in the art. The fine scan, being

preferably thus restricted to the ROI, can be executed in a shorter time than would be required to image the entire breast at a fine level of resolution.

Paragraph between page 7, line 21 and page 8, line 4:

After the historical and new images are aligned, they are compared in step 64 on a point-by-point basis, to obtain a <u>temporal</u> difference image which emphasizes the temporal changes which have occurred. <u>A temporal difference image provides a scalar or reinforcement metric of learning, whereas a simple difference image simply determines whether or not a change has occurred. A temporal difference image is a reinforcement feedback signal indicating a scalar of how good/bad, how much change (vector), or how strongly (acceleration) an action is happening. The scalars may represent, for example, a natural change, or the effectiveness of a treatment.</u> For example, if digitized two dimensional images are considered, the images are preferably first normalized to a common average value, then corresponding pixels are subtracted and the <u>temporal</u> difference values stored in a corresponding position in a <u>temporal</u> difference image. Analogously, if three-dimensional imagery is available (which is greatly preferred), voxels at corresponding locations in the early and later images are subtracted one from the other, and the result stored in a voxel of a <u>temporal</u> difference (volume) image. (A "voxel" is a unit of graphic information that defines a small volume element in three-dimensional space. It is the three-dimensional analog of a "pixel" which defines an area element in two- dimensional space.) Thus, normalized before and after images can be subtractively compared, voxel-by-voxel, to obtain a three-dimensional <u>temporal</u> difference image which represents the <u>temporal</u> differences between the before and after images.

Paragraph at page 8, lines 5-25:

As a result of step 64, at least three images are available to the image processor 24: an early (historical) image; a current image; and a temporal difference image. These images are then combined and/or selected for display (step 66) in various ways, as directed by user input from input device 32. Finally, the resulting image or images are displayed (step 68) and preferably stored (step 70) and/or exported (step 72, preferably via the data network) . It is highly [preferably] preferable that the imagery be coded to emphasize [visual] temporal differences between the earlier and later images. For example, the temporal difference image can be coded in a distinct color for display based on correlation output values, then superimposed on the early image, the later image, or a composite. Various other conventional methods could be equivalently employed to visually emphasize temporal image differences. For example, in one variation the temporal difference image can be displayed in intermittent, flickering display superimposed on either of the historical or current images. Significantly, the invention easily detects temporal differences between the earlier and later images, visually displays the images, and visually emphasizes these temporal differences.

Paragraph at page 9, lines 16-32:

The success of the above described procedure depends in part upon the accuracy with which the earlier and later images are registered (in steps 56 and 62 of FIG. 2a and 2b) before comparison. Slight movement or deformation of the breast tissue or the scanning apparatus is to be expected between the earlier and later scans. The movement may include translation, rotation about any axis, or slight compression or expansion (in addition to biological tissue changes). To adequately register the images in step 56 or 62, therefore, a computationally practical and fast

method of registration is preferred. A preferred method of registration takes advantage of the specific computational abilities of an optical correlator (discussed in detail below in connection with FIG. 9). This preferred method (suitable for use in step 64 of FIG. [2a] 2b) is best described with reference to an example of a particular coordinate system, to aid in visualization.

Paragraph at page 12, lines 25-37:

As an alternative to collapsing the images by simple projection, as described above, a three-dimensional image can be processed to create a "discriminate filter." Such filters are known and facilitate registration by providing a correlation filter which a composite of many images which differ by rotation about an axis. This allows testing of multiple, rotated slices simultaneously, by correlation with a composite discriminate filter. Once a discriminate filter is determined with acceptable correlation (at least [equa] equal to a pre-defined level of correlation) an individual filter is then selected from the set of slices which was used to compose the composite. In some cases, this method can greatly accelerate the search for best correlation.

Paragraph at page 18, lines 3-31:

After the earlier and later ROI images are adjusted to best register them, they can be either combined by adding, voxel-by-voxel, or compared by subtracting, voxel-by-voxel. Temporal differences [Differences] between the images are easily highlighted by changing the color at voxels which show high variation between the dual images. FIG. 8 shows an example of one typical display of a combined image (in this case, a composite of earlier and later images, with temporal differences highlighted). The outline of the breast 22 is shown, with

highlighted suspected lesion 200 (simplified for illustration) as revealed by a recent ultrasonogram. Other more static regions of density 202 and 203 are shown, which would suitably be displayed in a neutral color or grey scale. The earlier lesion region 206 is surrounded by the later, larger lesion 200. Suitably the later region 200 would be highlighted, by example by display in a conspicuous color such as pink. The smaller lesion 206 (visible in the earlier historical image) would preferably be coded in a different color (for example, green). This three dimensional image, easily digitized and archived on computer readable media, provides easily readable documentation of the historical image changes, and can be retrieved for evidence of tissue changes. The image processor can also extract slices such as that cut by imaginary plane 302, and display the slice as a two-dimensional section for detailed inspection. Preferably, the processor is programmed to respond to user input so that any slice can be selected for display, or the user can sweep through multiple slices to view details of interest.

Paragraph between page 21, line 24 and page 22, line 1:

When the input the filter images have been written to the input and filter ports 210 and 212, the optical correlator produces an output image which is a two dimensional output correlation pattern having an optical peak or peaks (bright spot) at the position of greatest correlation between the collapsed sonographic image and the radiographic image. The degree of correlation is indicated by the intensity of the output signal. The position of the output peak on the two-dimensional matrix of the correlator output CCD indicates the translations or shifts of the images relative to one another. The output image is read from the output photodetector (CCD) 214 by the image processor 24 in the conventional manner, typically by shifting the CCD voltage values out sequentially in rows (or columns) and then digitizing,

the output levels. The peak amplitudes of the 2D array provide the extent of correlation (degree of correlation) between the images. This scalar information is a measure of the temporal difference, and can be used as a measure of knowledge between images and supports actions that lead to a successful treatment or evaluation.

Paragraph at page 29, lines 1-14:

An image processing system and method visually documents and displays changes between historical and later mammographic images, preferably in three dimensions. A composite image is created which visually emphasizes temporal differences between the historical and later images. Preferably three-dimensional, digitized images, displayable in various projections, are stored for archival purposes on computer readable media. An image processor preferably exploits an optical correlator to register the historical and later images accurately and provide correlation values as temporal scalars of the differences. The registered images are then compared, voxel-by-voxel, to detect temporal differences. The composite image is displayed with synthetic colors or other visual clues to emphasize apparent changes (for example, tumor growth or shrinkage).

Amended claims with insertions and deletions indicated:

1. (amended) A method of visually documenting historical changes in biological tissue, comprising the steps of:

(a) obtaining a first image of a region of tissue;

(b) after obtaining said first image, obtaining a second image of said region of tissue;

(c) digitally storing said first and second images as digitized first and second images;

(d) spatially adjusting at least one of said first and second digitized images to spatially register said images so that corresponding features in both images are mapped to corresponding positions; and

(e) creating from said first and second digitized images a derived image which visually emphasizes <u>temporal</u> differences between said first and second images, thereby visually emphasizing historical changes between said images.

9. (amended) The method of claim 1, wherein said step of creating a composite image comprises:

comparing an image intensity at a location in said first image with a respective intensity at a corresponding location in said second image, and

determining a <u>temporal</u> difference image value based upon the <u>temporal</u> difference between said image intensity at said location in said first image and the respective intensity at said corresponding location in said second image.

10. (amended) The method of claim 1, wherein said composite image visually emphasizes <u>temporal</u> image differences by representing various regions of said composite image in synthetic colors, based upon <u>temporal</u> image differences between the first and second images.

11. (amended) A method of creating a displayable composite mammographic image from a plurality of raw mammographic images, corresponding to earlier and later mammographic images, comprising the steps of:

(a) obtaining the earlier image of a region of tissue;

(b) obtaining the later image of substantially the same region of tissue;

(c) deriving a temporal difference image which represents changes between said earlier and later images; and

(d) combining at least one of said earlier and later images with said temporal difference image, to produce a composite image.

16. (amended) The method of claim 11, wherein said step of creating a composite image comprises:

spatially adjusting at least [on] one of said earlier and later images to aid in registering said images.

19. (amended) A system for enhancing imagery of bodily tissues by relating earlier and later images, comprising:

an image processor, programmed to: (a) receive said earlier and later images, (b) register the earlier and later images by controlling an optical correlator to find a position of correlation between said earlier and later images, [and] (c) derive a composite image from the earlier and later images, (d) compute temporal differences between said earlier and later images, and (e) emphasize said temporal differences in said composite image; and

an optical correlator coupled to said image processor and arranged to correlate said earlier and later images, and to output to said image processor a cross

correlation image which is indicative of the position of correlation of the processed images.

23. The method of claim 4, wherein said step of creating a composite image comprises:

comparing an image intensity at a location in said first image with a respective intensity at a corresponding location in said second image, and

determining a <u>temporal</u> difference image value based upon said correlation output values.